REMARKS

The Office Action of June 17, 2002 has been carefully considered and the following response prepared.

Applicants' attorney would like to thank Examiner Kubelik for the helpful telephone conference on September 11, 2002 during which the claims were discussed. Specifically, the scope of term "overexpressing" in the claims was discussed. Examiner Kubelik advised Applicants attorney that "overexpressing" was interpreted to mean increased activity of an enzyme in native plants as well as expression of a foreign coding sequence in a transgenic plant or cell. Examiner Kubelik advised Applicants' attorney that if Applicants desired to limit the claims to transgenic plants and cells amending the claims to recite a step of transforming plant cells or plants would accomplish this. Accordingly, new claim 72 which recites such a "transforming" step has been added to the application. New claim 73 depends from claim 72 and states that the nucleic acid sequence encodes SAT3.

At paragraph 4 of the Office Action, the Examiner maintained the objection to the specification because it contains hyperlinks and/or other forms of browser-executable code. Specifically, the Examiner objected to page 41, line 15 that contains the web address of an internet program. The substitute specification has been amended to delete http:// from the web address. Withdrawal of this objection is requested.

At paragraph 5 of the Office Action, the Examiner advised Applicants that the proposed drawing corrections submitted March 28, 2002 have been accepted and required

formal drawing in the reply to the instant Office Action. Corrected formal drawings incorporating are submitted with this reply in a separate paper to the Official Draftsman.

At paragraph 6 of the Office Action, the Examiner indicated that a substitute specification was still needed because the photocopy of the application as filed submitted in the response to the previous Office Action was not entered. A substitute specification incorporating the amendments made in the response filed March 11, 2002 to the previous Office Action, in compliance with 37 CFR 1.125(a) is submitted herewith. The substitute specification contains no new matter. All references to specific pages in the instant response are to the originally filed specification.

At paragraph 10 of the Office Action, the Examiner rejected claims 2-6, 12, 13, 17-20, 23-26 and 60-71 under 35 USC 112, first paragraph because the specification, while being enabling for methods of increasing the production of cysteine, glutathione, methionine and sulfur-containing derivatives of methionine in a plant by transformation with a gene encoding a cysteine-insensitive plant SATase, does not reasonably provide enablement for methods of increasing the production of such compounds in a plants by transformation with a nucleic acid encoding a cysteine-sensitive SATase, by mitochondrial transformation with the nucleic acid, for mutagenesis of a plant SATase, for transformation with a protein, or for chloroplast targeting via the use of an optimized transit peptide. The Examiner additionally indicated that the claims are not enabled for genes encoding SAT from plants other than Arabidopsis because neither the specification nor the references on pages 6-9 of the specification teaches any plant SAT other than Arabidopsis, and the specification does not describe the hybridization and wash

conditions or the PR conditions, or the probes or primers needed to isolate genes from any organism other than Arabidopsis.

Applicants again traverse this rejection.

As discussed in the specification at page 9, SAT is known to occur in cysteine-sensitive and cysteine-insensitive forms. At page 9, line 6 several cysteine-sensitive SATs, SAT2, SAT4 and SAT1, are disclosed. The ability of the cysteine-sensitive form of SAT, SAT1, to increase production of cysteine, glutathione and methionine in transgenic plants expressing SAT1 in the mitochondria is shown in Example 13 at pages 61 and 62. In Example 13, plants transformed with the entire SAT1 sequence (which includes the transit peptide, amino acids 1-63 as shown in Figure 4) showed a 2-to 6-fold increase in cysteine levels in comparison with control plants, a 4-fold increase in the amount of glutathione in the cells, and a 2-to 3-fold increase in the amount of methionine as compared to control plants. The specification thus provides a working example of overexpression of a cysteine-sensitive SAT resulting in increased cysteine, glutathione, methionine or sulfur-containing derivatives of methionine, and any unpredictability of the ability of embodiments of the claimed methods employing cysteine-sentsitive SAT is overcome.

With regard to mitochondrial transformation, claim 12 has been canceled without prejudice. Claim 13 indicates that a nucleic acid encoding a mitochondrial signal peptide/SAT fusion protein is used. Clam 13 has been amended to depend from claim 60 in view of the cancellation of claim 12.

With regard to claim 5, plant and bacterial SATs that have been rendered cysteine-insensitive by mutagenesis are referred to in the specification at page 9, lines 22-

27 and the references cited therein. The cited references clearly show which part of the sequences can be modified to change the SAT from cysteine-sensitive to cysteine-insensitive, and the teachings of these publications can be applied to plant SATs to change a cysteine-sensitive SAT to a cysteine-insensitive SAT without undue experimentation.

With regard to transformation by a protein, as suggested by the Examiner, claim 60 has been amended to state that the plant cells are transformed with a nucleic acid sequence encoding a SAT.

With regard to the Examiner's assertions that the optimized transit peptide (OTP) is not enabled because neither EP 508 909 (cited in the specification at page 14, lines 16-28 and page 15, lines 1-5), nor the specification teach the DNA sequence that encodes the OTP, the Examiner's attention is drawn to the U.S. patents RE36, 449 and RE37, 287, which are U.S. equivalents of EP 508 909. Copies of RE36, 449 and RE37, 287 are submitted for the Examiner's attention with this response. EP 508 909, RE36, 449 and RE37,287 describes the construction of the OTP using portions of the cloned cDNA of the small subunit of the maize RuBisCO gene the sequence of which was disclosed in LeBrun *et al.* Nucleic acids Research 15: 4360 (1987) and from the cloned cDNA of the small subunit of the sunflower RuBisCO gene the sequence of which was disclosed in Waksman *et al.* Nucleic Acids Research 15: 7181 (1987), copies of both of which are submitted for the Examiner's attention. The specification thus enables the OTP. The nucleic acid sequences making up the OTP are known in the art. EP 508 909 (and the corresponding U.S. patents) discloses construction of the OTP from these known sequences.

In the previous Office Action, the Examiner indicated that the use of any transit peptide was unpredictable based on the disclosures of Turk *et al.*, New Phytol. 136: 29-38 (1997). Turk *et al.* does not support the Examiner's arguments that targeting sequences are themselves unpredictable. Turk *et al.* discloses experiments using the *Ipomoea batata* sporamin vacuolar targeting signal to transport the reporter enzyme GUS and bacterial levansucrase (which synthesizes fructans) into vacuoles of transgenic plants. The authors found that a fusion protein of the N-terminal 111 amino acids of sporamin (which contains the signal peptide) and GUS was translocated into vacuoles, but that a fusion protein of the N-terminal 111 amino acids of sporamin and levansucrase was not transported into vacuoles. At page 36, left hand column, the authors noted that the sporamin/levansucrase fusion protein was properly translocated to the endoplasmic reticulum, but was not properly transferred to the vacuole. The authors indicated that the structure of the levamsucrase protein itself was responsible for the failure of the fusion protein to be transferred to the vacuole, rather than any defect in the ability of the sporamin vacuolar transit peptide to direct heterologous proteins to the vacuole.

In contrast to the situation in Turk *et al.*, Applicants have demonstrated in the examples in the specification that SAT can be successfully transported to mitochondria and chloroplasts. The Examiner has provided no valid reasons to support the assertion that transit peptides are themselves unpredictable and this portion of the present rejection is therefore improper.

With regard to the portion of the present rejection relating to enablement of SATs from plants other than Arabidopsis, Applicants again assert that the specification enables the use of SATs from plants other than Arabidopsis in the claimed methods. Prior to

filing the present application, SATs had been well-characterized in bacteria and plants, and a number of references to cloned SATs are cited in the specification at pages 6 and 9. The Arabidopsis sequences disclosed in the specification were isolated from Arabidopsis by functional complementation of an E. coli strain deficient in SAT activity in accordance with the method described in Ruffet *et al.*, Eur. J. Biochem. 227: 500-509 (1995). See Examples 2, 5, 7 and 8 in the specification. In these examples, Ruffet *et al.* is disclosed as reference [12]. The full citation for Ruffet *et al.* is shown at page 6, lines 23-24. The functional complementation method can be used to obtain SAT from plants other than Arabidopsis. This method does not depend on any specific primers, probes, PCR conditions or wash conditions. In addition to Arabidopsis, this method has been used to obtain a nucleotide sequence encoding SAT from watermelon (Saito *et al.*, J. Biol. Chem. 270: 16321-16326 (1995)). The specification therefore enables nucleotide sequences encoding SAT obtained from plants other than Arabidopsis.

In view of the above, withdrawal of this section 112, first paragraph rejection is requested.

At paragraph 11 of the Office Action, the Examiner rejected claims 17, 19, 23, 25, 60 and 70-71 under 35 USC 112, first paragraph because the use of a plasmid containing an optimized transit peptide is not enabled and hence the invention is not enabled. This rejection is repeated from the previous Office Action.

Applicants again traverse this rejection.

Deposits of biological material may be necessary to satisfy the requirements of 112, first paragraph where the invention involves a biological material and words alone cannot sufficiently describe how to make and use the invention in a reproducible manner.

However, in accordance with 37 CFR 1.802(b), a deposit is not necessary if the material is known and readily available to the public or can be made or isolated without undue experimentation.

The specification discloses the optimized transit peptide of EP 508 909 at page 14, lines 16-28 and page 15, lines 1-5. This is the OTP shown the plasmid in Figure 11 and referred to in Example 9 at page 43 of the specification. As discussed above, EP 508 909, RE36, 449 and RE37, 287 describe the construction of the OTP using portions of the cloned cDNA of the small subunit of the maize RuBisCO gene the sequence of which was disclosed in LeBrun *et al.* Nucleic acids Research 15: 4360 (1987) and the cloned cDNA of the small subunit of the sunflower RuBisCO gene the sequence of which was disclosed in Waksman *et al.* Nucleic Acids Research 15: 7181 (1987). The nucleotide sequence of the OTP is therefore known and readily available to the public and no deposit of biological material is necessary to satisfy the requirements of section 112, first paragraph. Withdrawal of this section, 112, first paragraph rejection is requested.

At paragraph 12 of the Office Action the Examiner rejected claims 2-6, 12-13, 17-20, 23-26 and 60-71 under 35 USC 112, first paragraph as because they contain subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. This rejection is repeated from the previous Office Action. The basis for the rejection in the present Office Action is that the specification does not teach SAT genes from any plant other than Arabidopsis, mutant SAT genes and cysteine-insensitive SATs from any plant, or the sequence of an OTP.

Applicants again traverse this rejection. In order to satisfy the written description requirement of 112, first paragraph, the Applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the "written description" inquiry, whatever is claimed. *Vas Cath Inc. v. Mahurkur* 19 USPQ2d 1111, 1117 (Fed. Cir. 1991). One shows that one is "in possession" of the invention by such descriptive means as words, structures, figures, diagrams, formulas, etc. that fully set forth the claimed invention. *Lockwood v. American Airlines* 41 USPQ2d 1961, 1966 (Fed. Cir. 1997).

The portion of *In re Shokal* 113 USPQ 283 (CCPA 1957) cited by the Examiner in the present Office Action does not support the Examiner's assertion that the instant specification provides inadequate written description. In *In re Shokal*, the Applicants were claiming support in a prior filed application for a claim in a later application. The genus representing the claim was not identified in the prior application, but support was instead drawn from examples and various general disclosures, some of which read on the prior art. The description in the earlier application was found insufficient to support the claims in the later application because, as stated in the last sentence of the part of *In re Shokal* set out in the Office Action, "... four species might be held to support a genus, if such genus is disclosed in clear language, but where those species must be relied upon not only to illustrate the genus, but to define what it is, the situation is otherwise.

In contrast to the situation in *In re Shokal*, the instant specification describes the present invention in clear language that conveys with reasonable clarity to those skilled in the art that the inventors were in possession of the claimed invention when the application was filed. The specification at pages 9 and 10 discloses that the

overexpressed SAT can be any SAT, whether of plant, bacterial or other origin, and provides examples of SATs suitable for use in the invention, including cysteine-sensitive and cysteine-insensitive forms of SAT, and cytoplasmic, mitochondrial and chloroplast forms of SAT. The specification thus discloses the genus in clear terms, and the species disclosed are illustrative, and not used to define the genus. In addition to SAT3 (SEQ ID NO: 1), the application discloses the sequences of five other SATs. Persons skilled in the art can readily substitute any other SAT for the ones disclosed in the specification by referring to the scientific literature and databases, which one skilled in the art would be led to do so because of the disclosure in the specification that any SAT is useful in the claimed methods. For example, Saito *et al.*, Gene 189: 57-63, 1997, cited in the present Office Action, discloses the nucleotide and amino acid sequence of a cytoplasmic SAT from watermelon.

Similarly, the plant and bacterial SATs that have been rendered cysteine-insensitive by mutagenesis are referred to in the specification at page 9, lines 22-27 and the references cited therein. The cited references clearly show which part of the sequences can be modified to change the SAT from cysteine-sensitive to cysteine-insensitive, and the teachings of these publications can be applied to plant SATs to change a cysteine-sensitive SAT to a cysteine-insensitive SAT without undue experimentation.

With regard to the OTP, the specification discloses the OTP of European patent application EP 508 909 at page 14, lines 16-28 and page 15, lines 1-5. As discussed above, EP 508 909, RE36, 449 and RE37, 287 describe the construction of the OTP using portions of the cloned cDNA of the small subunit of the maize RuBisCO gene the

sequence of which was disclosed in LeBrun *et al.* Nucleic acids Research 15: 4360 (1987) and the cloned cDNA of the small subunit of the sunflower RuBisCO gene the sequence of which was disclosed in Waksman *et al.* Nucleic Acids Research 15: 7181 (1987).

The specification conveys with reasonable clarity to those skilled in the art that, as of the filing date sought, the inventors were in possession of the invention. Withdrawal of this section 112, first paragraph rejection is requested.

At paragraph 13, the Examiner rejected claims 2-6, 9, 12-13, 17-20, 23-26 and 60-71 under 35 USC 112, second paragraph as indefinite. This rejection contains several sections, each of which will be answered separately.

The Examiner rejected claim 4 because it contains the abbreviation SAT, for the reasons stated in the previous Office Action. The abbreviation "SAT" does not appear in claim 4. However, "SAT" has been deleted from claim 5 and replaced with "serine acetyltransferase".

The Examiner maintained the rejection of claim 26 because it contains the abbreviation "EPSPS" and EPSPS is not defined in the specification. Applicants again traverse this rejection. EPSPS is the well-known abbreviation for 5-enolpyruvylshikim-ate-3-phosphate synthase. EPSPS catalyzes the conversion of shikimate-3-phosphate into 5-enolpyruvyl-shikimate-3-phosphate, an intermediate in the biochemical pathway for creating three essential aromatic amino acids (tyrosine, phenylalanine, and tryptophan). The herbicide glyphosate acts by inhibiting this enzyme. The specification at page 13, lines 26-26 states that a plant EPSPS transit peptide is described in EP 218 571. EP 218, 571, published April 15, 1987, refers to 5-enolpyruvylshikimate-3-

phosphate synthase on page 1 as EPSPS and uses the abbreviation EPSPS throughout to refer to this enzyme. Additionally, U.S. patents RE36, 449 and RE37, 287 use the abbreviation EPSPS for 5-enolpyruvylshikimate-3-phosphate synthase in column 1. The abbreviation EPSPS in claim 26 is well known in the art as shown by its use in the patents above and its use in claim 26 does not render the claim indefinite.

Claims 20 and 23 were again rejected because of the use of the term "homologous" and "heterologous", respectively. Claim 20 has been amended to state that the fusion protein is the naturally expressed fusion protein. Claim 23 has been amended to state that the serine acetyltransferase and the transit peptide of the fusion protein are from different proteins. Support for these amendments can be found in the specification at page 13, lines 9-20.

Claim 60 was rejected as indefinite in the recitation of the phrase "plant cells transformed with a serine acetyltransferase" because plants are not transformed with proteins but with nucleic acids. Claim 60 has been amended to state that the plant cells are transformed with a nucleotide sequence encoding serine acetyltransferase.

In view of the above, withdrawal of the entire section 112, second paragraph rejection is requested.

At paragraph 14, the Examiner rejected claims 2-6, 12-13, 17, 19-20, 23-26 and 60-71 under 35 USC 103(a) as being unpatentable over Saito *et al.*, Plant Physiol. 106: 887-895, 1994 in view of Noji *et al.*, JBC 273:32739-32745, 1998, for the reasons set for the in the Office Action mailed September 10, 2001, as applied to claims 1-6, 8, 12-12, 17, 19-20 and 23-30. Briefly, the basis for this rejection is that it would have been obvious to one of ordinary skill in the art to increase the production of cysteine in a plant

by overexpressing a cytoplasmic cysteine synthase in the cytoplasm and chloroplasts of a plant as taught by Saito *et al.* and to modify that to use another enzyme required for cysteine biosynthesis, SAT, as described in Noji *et al.* and that one skilled in the art would be motivated to do so because of the role SAT has in regulation of cysteine biosynthesis and because substitution of one crucial enzyme for cysteine biosynthesis for another crucial enzyme for cysteine biosynthesis is an obvious design choice.

In the present Office Action, the Examiner pointed out portions of Saito et al. that allegedly support the finding of an increase in cysteine production (page 891, left column, paragraph 1) and overexpression of SAT (page 893, left column, paragraph 1).

Applicants again traverse this rejection. As discussed in Applicants' response to the previous Office Action, Saito *et al.* discloses overexpression of cysteine synthase in tobacco plants transformed to express spinach cytoplasmic cysteine synthase. In the present Office Action, in response to Applicants' arguments in the response to the previous Office Action that Saito *et al.* found no significant changes in cellular content of cysteine and glutathione in the transgenic plants, the Examiner cited the phrase "an increase in 3F and 4F plants was observed" at page 891, left column, first paragraph as supporting the assertion that Saito *et al.* obtained increased levels of cysteine and glutathione in the transgenic plants.

The phrase "an increase in 3F and 4F plants was observed" was taken out of context and, when read in with the remainder of the sentence and paragraph from which it was taken, does not support the conclusion that Saito *et al.* found increased levels of cysteine and glutathione in transgenic plants overexpressing cysteine synthase. Saito *et*

al., page 890, right column, last paragraph which runs through page 891, left column, first paragraph states:

> Cellular contents of Cys and GSH in the transgenic plants grown aseptically in A1 agar medium were determined to be within the range reported previously (Giovanelli *et al.* 1990, Rennenberg, 1982) (Fig. 5). No significant changes in the contents of these sulfhydryl metabolites, in contrast with the differences in CSase activity, were seen among transformants of different constructs and control plants, although some tendency toward an increase in 3F and 4F plants was observed. This suggested that under normal growth conditions without sulfur stress the cellular contents of Cys and GSH were stationary and not directly influenced by increased cellular CSase activity.

When taken in context, Saito *et al.* discloses that there were no significant changes in the amounts of cysteine and glutathione in the transgenic plants, the amounts of these two metabolites being within the range previously reported.

Also in the present Office Action, in response to Applicants' previous arguments that Noji *et al.* does not suggest overexpression of SAT in plants to increase production of cysteine, the Examiner cited page 893, left column, first paragraph as suggesting overexpression of SAT. This paragraph of Saito *et al.* discusses a working model for the regulatory mechanism of cysteine biosynthesis in chloroplasts accumulating overexpressed cysteine synthase. There is no suggestion in this paragraph for overexpressing SAT. The only possible relevant sentence states: "Overexpressed CSase in the transgenic plants may require more Ser acetyltransferase, leading to enhanced availability of OAS for maximal Cys formation." This sentence falls far short of suggesting overexpression of SAT, and, even if it could be construed to suggest

overexpression of SAT, can only mean that both cysteine synthase and SAT must be overexpressed for maximal cysteine formation.

Noji *et al.* discloses experiments on the subcellular localization of SAT and feed back regulation of the three SAT forms from *A. thaliana*. Experiments were performed using *E. coli* or plants transformed with fusion proteins comprised of an SAT N-terminal fragment fused to jellyfish green fluorescent protein (GFP). Noji *et al.* discusses the putative role of SAT in regulation of cysteine biosynthesis by analogy to bacterial SAT. There is no suggestion in Noji *et al.* that overexpression of SAT in plant cells would increase production of cysteine, much less a suggestion that it would be an obvious design choice to substitute SAT for cysteine synthase to increase cysteine production.

It is well-established that before a conclusion of obviousness may be made based on a combination of references, there must be a reason, suggestion or motivation in the prior art to lead an inventor to combine those references. Saito *et al.* discloses experiments using a different enzyme, cysteine synthase. Saito *et al* does not disclose a method of increasing cysteine production in plants, much less suggest that SAT could be substituted for cysteine synthase. (As discussed above, Saito *et al.* found no significant changes in cysteine and glutathione levels in transgenic plants overexpressing cysteine synthase.) At best, Saito *et al.* arguably suggests overexpression of both cysteine synthase and SAT. Noji *et al.* does not cure the deficiencies of Saito *et al.* Noji *et al.* discloses experiments of feedback regulation and subcellular localization of SAT, but does not suggest that overexpression of SAT in plant cells could increase production of cysteine or suggest. There is thus no suggestion, reason or motivation in the prior art to

modify the teachings of Saito *et al.* to substitute overexpression of SAT, disclosed in Noji *et al.*, for cysteine synthase to increase production of cysteine.

Even assuming *arguendo* that the combination of references is proper, the combined disclosures of the references are insufficient to support the Examiner's conclusion that the claimed methods of increasing the production of cysteine is obvious. The combined disclosures of Saito *et al.* and Noji *et al.* still fail to suggest that cysteine production could be increased by overexpressing SAT alone in plant cells. The combined disclosures of Saito *et al.* and Noji *et al.* at best suggest that overexpression of both cysteine synthase and SAT are necessary to obtain increased production of cysteine and glutathione, even if such an increase would be possible.

Saito *et al.* failed to obtain significant increase in production of cysteine and glutathione in transgenic plants transformed with cysteine synthase. One skilled in the art would not be motivated to substitute a different enzyme for cysteine synthase with the reasonable expectation of increasing the production of cysteine and glutathione because overexpression of cysteine synthase failed to significantly increase the production of these two compounds, and there is no suggestion in Saito *et al.* or Noji *et al.* that the result would be different with another enzyme, let alone a different result with overexpression of SAT alone.

The Examiner's reasons for combining Saito *et al.* and Noji *et al.* amount to an impermissible hindsight reconstruction of Applicant's invention and do not stem from the prior art. Synthesis of cysteine in plants depends on a number of enzymes and requires the availability of biosynthetic precursors. In addition, sulfate transporters play an important role. Given this complex regulation of sulfur assimilation, the present

invention surprisingly shows that the overexpression of a single enzyme, SAT, allows increased production of sulfur-containing amino acids in plants.

The method of new claim 72 is not disclosed or suggested by the combined disclosures of Saito et al. and Noji et al. for the reasons discussed above. There is no suggestion in the combined references of transforming plant cells with a nucleotide sequence encoding a serine acetyltransferase, and expressing the nucleotide sequence encoding a serine acetyltransferase in the plant cells or in a plant containing the plant cells, whereby expression of the nucleic acid sequence results in the increased production of cysteine, methionine, glutathione, methionine or sulfur-containing derivatives of methionine in the plants cells or plant.

Withdrawal of this section 103 rejection is again requested.

At paragraph 15 of the Office Action the Examiner maintained the rejection of claim 18 under 35 USC 102(a) as being unpatentable over Saito et al. (1994) in view of Noji et al. at applied to claims 2-6, 12-13, 17, 19-20, 23-26 and 60-71 and further in view of Svab et al. for the reasons set out in the Office Action of September 10, 2001.

Saito et al. and Noji et al. were discussed above.

Svab *et al.* discloses increased frequency of plastid transformation using a plasmid containing a tobacco *Sac*II-*Eco*RV plastid fragment wherein a chimeric gene is inserted between the rbcL gene and open reading frame ORF512. Svab *et al.* has nothing in common with the present invention beyond the disclosure of a method for transforming chloroplasts that could be used transform chloroplasts with SAT.

The addition of Svab *et al.* does not cure the deficiencies of Saito *et al.* and Noji *et al.* The combined disclosures of Saito *et al.*, Noji *et al.* and Svab *et al.* still fail to

suggest Applicants' claimed method of increasing production of cysteine, glutathoine, methionine or sulfur-containing derivatives of methionine by overexpressing SAT in plant cells transformed with a nucleic acid sequence encoding SAT or plants containing such plant cells. Claim 18 is not obvious over Saito *et al.* in view of Noji *et al.* and Svab *et al.* Withdrawal of this section 103(a) rejection is again requested.

In view of the above, the present application is believed to be in a condition ready for allowance. Entry of the amendments to the claims is requested as they are believed to place the claims in conditions for allowance or at least better form for appeal. Reconsideration of the application is respectfully requested and an early Notice of Allowance is earnestly solicited.

Respectfully submitted,
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Marked Up Amended Substitute Specification

[0107] Analysis of the N-terminal portion of the sequence shows the presence of characteristics for addressing of the protein to an organelle (mitochondrion or chloroplast). Unlike the other isoforms described above, the SAT2 gene is complex and has several introns. Comparing SAT2 sequences with its homologues from *A. thaliana*, from plants and from other organisms, leads to the assumption of a prokaryotic origin (**Figure** 10). Moreover, analysis of the N-terminal sequence using the chloroP program [~~http://~~www.cbs.dtu.dk/services/chlorP/], indicates a high probability of the presence of a chloroplast-type transit peptide.

Marked Up Version of Amended Claims

5. (twice amended) Method according to claim 4, characterized in that the serine acetyltransferase is a plant [SAT] serine acetyltransferase, a bacterial serine acetyltransferase, a plant [SAT] serine acetyltransferase rendered cysteine-insensitive by mutagenesis or a bacterial serine acetyltransferase rendered cysteine-insensitive by mutagenesis.

13. (twice amended) Method according to [claim 12] claim 60, characterized in that the serine acetyltransferase is overexpressed in the cytoplasm in the form of a mitochondrial signal peptide/ serine acetyltransferase fusion protein, the mature functional serine acetyltransferase being released inside mitochondria.

20. (twice amended) Method according to claim 19, characterized in that the [serine acetyltransferase and transit peptide of the] fusion protein [are homologous] is the naturally expressed fusion protein.

23. (twice amended) Method according to claim 19, characterized in that the serine acetyltransferase and the transit peptide of the fusion protein are [heterologous] from different proteins.

60. (amended) A method for increasing the production of cysteine, glutathione, methionine or sulfur-containing derivatives of methionine by plant cells and plants, said method comprising overexpressing serine acetyltransferase in plant cells transformed with a nucleic acid sequence encoding a serine acetyltransferase or in plants containing said plant cells, whereby overexpression of serine acetyltransferase results in the

increased production of cysteine, methionine, glutathione, methionine or sulfur-containing derivatives of methionine.